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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,538	10/06/2005	John F. Wikswo	14506-48684	7090

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EXAMINER

EDWARDS, LYDIA E

ART UNIT	PAPER NUMBER
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1797

NOTIFICATION DATE	DELIVERY MODE
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12/30/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/525,538

Applicant(s)

WIKSWO ET AL.

Examiner

LYDIA EDWARDS

Art Unit

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-77 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-77 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 February 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/GA-6)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date See Continuation Sheet

Continuation of Attachment(s) 3. Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :4/12/2006, 7/17/2006, 9/26/2006, 4/2/2007, and 8/3/2007.

DETAILED ACTION

Claim Objections

Claims 40-41 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 40 and 41 duplicate claims 31 and 32 and therefore, do not further limit claim 28.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5, 8-16, 19-22, 33-38, 41-48 and 50-65 are rejected under 35 U.S.C. 102(a) as being anticipated by Kanegasaki WO 02/46355 (US 20030003571 has been used as an English equivalent and cited herein after).

Regarding Claims 1-8, 18, 21, 23 and 49-56, Kanegasaki ('571) discloses a bioreactor for cultivating cells in a liquid medium comprising a first substrate (Figure 5:7) having first and second surfaces defining a chamber therebetween. A barrier comprising a channel (Figure 5:1) and a plurality of protrusions (Figure 5:6) serve to divide the chamber into a first subchamber (Figure 5:2A) and a second subchamber (Figure 5:2B). This is disclosed in paragraphs [0084], [0085] and [0095]. Paragraph [0097] states that the protrusions and grooves formed within the channels are varied in order to control the diffusion of a particular cell type between the subchambers. Paragraph [121] states that the gaps of the barrier range from 3 to 50 microns. Figure 12 and paragraph [112] describe another configuration in which first and second barriers (1) are positioned so as to form a central chamber (2A), an intermediate chamber (2B), and an

outer chamber (2C). Furthermore, Kanegasaki teaches that an input port (Figure 3:3Aa) and an input transfer channel are formed in the substrate and provided in fluid communication with the first subchamber. Furthermore, an outlet port (Figure 3:3Ba) and an outlet transfer channel are provided in communication with the second subchamber.

Regarding Claims 4-7 and 52-55, Kanegasaki ('571) disclose the bioreactor set forth in claims 1 and 49. The bioreactor disclosed by Kanegasaki is considered to be fully capable of accommodating any type of microorganism including bacteria, protozoa, tumor cells, endothelial cells, and normal tissue cells.

Regarding Claims 13, 15 and 61, Kanegasaki ('571) disclose the bioreactor set forth in claim 1 and 49 wherein at least one auxiliary port and channel are provided in fluid communication with the input and outlet ports. Kanegasaki teaches that additional ports (Figure 3:4Ba and Figure 3:4Aa) are used in conjunction with inlet (Figure 3:3Aa) and outlet (Figure 3:3Ba) ports, so as to supply extra reagents to the subchambers.

Regarding Claims 14, 16-17, 20, 22, 29-30, 39, 42-43, 48 and 75, with respect to the intended use limitations, the device disclose by Kanegasaki, is structurally the same as the instantly claimed and is capable of providing the operating conditions listed in the intended use section of the claim. Note statements of intended use carry no patentable weight when the structure of the Claim has been met by the prior art reference.

Regarding Claims 25, and 63, Kanegasaki ('571) discloses wherein the first substrate is formed from silicon (Paragraph 154).

Regarding Claims 44 and 71, Kanegasaki ('571) discloses a means positioned in the channel and adapted for monitoring of the cells therein (Paragraphs 163-164).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-12 and 57-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571)) as applied to claims 1 and 49, and further in view of Griffith et al. (US 6197575).

Regarding Claims 9-12 and 57-60, Kanegasaki ('571) does not expressly disclose the use of cell adhesion coatings.

Griffith ('575) teaches that it is known in the art to modify surface properties by applying biocompatible coatings to the surfaces in order to promote cell adhesion or inhibit cell adhesion (Col 17, lines 28-39 and Col 18, lines 10-16).

At the time of the invention, it would have been obvious to utilize the surface modification disclosed by Griffith in the apparatus set forth by Kanegasaki. In paragraph 160, Kanegasaki teaches that materials that encourage cell adhesion to substrate surfaces are beneficial. One of ordinary skill in the art would have recognized that the application of a coating to the substrate of Kanegasaki would have required only minor structural alterations, and would be completed in a predictable manner while yielding predictable results.

Claims 19 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571)) as applied above to claims 1 and 49, further in view of Sparks (US 5157438).

Regarding Claims 19 and 24, Kanegasaki ('571) discloses a cover cap (Figure 39:17) but does not expressly disclose wherein the cover cap is adapted for slidably covering or opening the open end of the sample chamber.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Kanegasaki with a cover for slidably covering or opening the

sample chamber since Sparks ('438) discloses that it was known in the art at the time the invention was made to provide a cover (lid) which can slidably engage covering or opening a sample chamber (Col 3, lines 1-7).

Claims 26-31 and 64-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) as applied above to claims 1 and 49, further in view of Lynes (US 20020086280).

Regarding Claims 26-31 and 64-69, Kanegasaki ('571) disclose the bioreactor set forth in claim 1 and 49. Kanegasaki, however, does not expressly disclose a means for electrochemical measurements. Furthermore, Kanegasaki does not disclose a multiplexed potentiostat.

Lynes discloses a substrate (Figure 1:58) designed to monitor cell movement in response to chemotactic factors. Paragraphs [18] and [19] indicate that a plurality of individually addressable working electrodes (Figure 1:10) and counter electrodes are arrayed upon the substrate so as to measure changes in impedance, resistance or capacitance that result from the motion of cells (Figure 1:54). Lynes further describes the use of at least one reference electrode. Figure 2 indicates that a plurality of edge connector pads and electrically conductive leads are in communication with each electrode. The effect of a certain analyte is determined by monitoring cell behavior upon the introduction of the analyte into the culture solution.

At the time of the invention, it would have been obvious to provide the system of Kanegasaki with a plurality of electrodes capable of detecting cell movement. This would allow for a second means to determine cell behavior in addition to simple visual observation. Generally speaking, automated detection using impedance measurements is often times superior to visual observation, which is difficult and laborious. Paragraph [0017] of Lynes teaches that electrical detection using a patterned array of electrodes offers a rapid, automated and multiplexed analysis of cell movement and factors capable of affecting such movement.

Claims 26-31 and 64-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Lynes (US 20020086280) as applied above to claims 31 and 69, further in view of Henkens et al. (US 6391558).

The combination of Kanegasaki, and Lynes do not disclose a multiplexed potentiostat.

Henkens et al. ('558) disclose an electrochemical detection device which comprises a multiplexed potentiostat (Col 5, lines 3-8).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Kanegasaki, and Lynes with a multiplexed potentiostat as taught by Henkens in order to measure the current of different targets.

Claims 33-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Lynes (US 20020086280) as applied above to claims 28, further in view of Quake (US 20020164816).

Regarding Claims 33-36, Kanegasaki ('571) does not disclose a plurality of controlling ports comprising a fluid control valve.

Quake ('816) teaches that pumps and valves generally are designed to control the movement and direction of fluids containing such materials within flow channels of the microfluidic devices. Generally, pump and valve systems employ pressure or other known actuation systems to affect fluid movement and direction in flow channels. Other fluid movement and direction controls for microfluidic devices are known in the art, including mechanical pumps and valves (Paragraph 206).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Kanegasaki with a control port since Quake ('816) discloses that it was known in the art at the time the invention was made to provide fluid movement and direction controls.

Regarding Claims 37-39, it would have been obvious to one having ordinary skill in the art at the time the invention was made to position the counter electrode and working electrode between the fluid control valve and controlling port, since it has been held that rearranging parts of an invention involves only routine skill in the art. *In re Japikse*, 86 USPQ 70.

With respect to the intended use limitations, the device disclosed by the combination of Kanegasaki, Lynes, and Quake, is structurally the same as the instantly claimed and is capable of providing the operating conditions listed in the intended use section of the claim. Note statements of intended use carry no patentable weight when the structure of the Claim has been met by the prior art reference.

Claims 45-46 and 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Rao (US 20020025547).

Regarding Claims 45-46 Kanegasaki teaches a monitoring means; however, he does not explicitly state wherein the means for monitoring of the cells comprises at least one optical sensor and at least one lead in optical communication with a corresponding optical sensor.

Rao ('547) discloses an optical chemical sensor which is excited by a light emitting diode wherein detection can occur via optical fibers coupled to a single diode array (Paragraphs 78-90).

At the time of the invention, it would have been obvious to provide the Kanegasaki device with an optical sensor, LED light sources and other optical detection means well known in the art. As evidenced by Rao, it is well known in the art to provide a bioreactor with an optical sensing system.

Claims 47 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Anderson et al. (US 6168948).

Regarding Claims 47 and 74 Kanegasaki does not disclose wherein the means for monitoring of the cells comprises at least one electrical sensor and at least one lead in electrical communication with a corresponding electrical sensor.

Anderson et al. ('948) discloses at least one electrical sensor and at least one lead in electrical communication with a corresponding electrical sensor (Col 43, line 65-Col 44, line 5).

At the time of the invention, it would have been obvious to provide the Kanegasaki device with an electrical sensor. As evidenced by Anderson, it is well known in the art to use an electrical sensor to monitor the various reactions.

Claim 76 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Herman et al (US 20010044143).

Regarding Claims 76, Kanegasaki ('571) discloses a bioreactor for cultivating cells in a liquid medium comprising a first substrate (Figure 5:7) having first and second surfaces defining a chamber therebetween. A barrier comprising a channel (Figure 5:1) and a plurality of protrusions (Figure 5:6) serve to divide the chamber into a first subchamber (Figure 5:2A) and a second subchamber (Figure 5:2B). This is disclosed in paragraphs [0084], [0085] and [0095]. Paragraph [0097] states that the protrusions and grooves formed within the channels are varied in order to control the diffusion of a particular cell type between the subchambers. Paragraph [121] states that the gaps of the barrier range from 3 to 50 microns. Figure 12 and paragraph [112] describe another configuration in which first and second barriers (1) are positioned so as to form a central chamber (2A), an intermediate chamber (2B), and an outer chamber (2C). Furthermore, Kanegasaki teaches that an input port (Figure 3:3Aa) and an input transfer channel are formed in the substrate and provided in fluid communication with the first subchamber. Furthermore, an outlet port (Figure 3:3Ba) and an outlet transfer channel are provided in communication with the second subchamber. Kanegasaki does not disclose the use of biofilms.

Herman et al. ('143) disclose the use of biofilms in Paragraph 45.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Kanegasaki to include biofilms since Herman ('143) discloses that it was known in the art at the time the invention was made to provide biofilms.

Claim 77 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Herman et al (US 20010044143) as applied above to Claim 76, further in view of Turner et al. (US 5624537).

Regarding Claim 77, Kanegasaki does not disclose the use of a bolus of selected chemicals.

Turner et al. ('537) discloses the use of a bolus of chemicals (Col 18, line 61-61 and Col 19, lines 6-7).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Kanegasaki to include a bolus of chemicals and or reagents since Turner ('537) discloses that it was known in the art at the time the invention was made to provide a bolus of chemicals.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LYDIA EDWARDS whose telephone number is (571)270-3242. The examiner can normally be reached on Mon-Thur 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Walter Griffin can be reached on 571.272.1447. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LYDIA EDWARDS/
Examiner
Art Unit 1797

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Supervisory Patent Examiner, Art Unit 1797